REMARKS

I. Support for Amendments

The sequence listing was amended to change the description of the organism for SEQ ID NO: 3 from "murine sp" to "mouse". This amendment is supported by the sequence listing which was originally filed on February 2, 2000 as well as the description of Figure 3 on page 6 of the specification. Claims 69-74 and 78 were amended to more clearly define the invention. Support for these amendments is found throughout the specification, for instance, on page 7, line 24 to page 8, line 2, and pages 19-21. Accordingly, no new matter is added by this Amendment and entry thereof is respectfully requested.

II. Response to Election/Restrictions

The Examiner asserts that newly submitted claims 73-78 are directed to an invention that is independent or distinct from the invention originally claimed. Specifically, the Examiner asserts that claims 73 and 74 are directed to polypeptides and glycopolypeptides comprising materially different amino acid sequences as evidenced by separate amino acid position substitutions. Applicants respectfully traverse this objection as claims 73 and 74 contain the same amino acid position substitutions, albeit a smaller subset, as pending claims 71 and 72. Therefore, Applicants respectfully request that this objection be withdrawn and these claims be allowed.

The Examiner has also asserted that claims 75-78 are directed to a *human ovarian cell* containing a vector; therefore, the Examiner asserts that they are directed to an invention that is

independent or distinct from the invention originally claimed. Applicants respectfully disagree with the Examiner's characterization of these claims as they are actually directed to a *ZP3 protein* expressed by an ovarian cell. Therefore, Applicants submit that claims 73-78 are not directed to a non-elected invention and should not be withdrawn from consideration under 37 CFR 1.142(b).

II. Objection to the Specification

The Examiner has objected to the substitute raw sequence listings filed November 14, 2000 and May 18, 2004 under 35 U.S.C. 132 as he asserts that they introduce new matter into the disclosure because the description of the organism was changed from "mouse" to "murine sp" for SEQ ID NO: 3. Applicants have amended the sequence listing so that "mouse" is recited as the organism for SEQ ID NO: 3. Therefore, Applicants respectfully request that this objection be withdrawn.

The Examiner has also objected to the specification because of Applicants' reference to Table 1. The Examiner asserts that there is no such table of record. Applicants respectfully submit that Table 1 is located on page 30 of the originally filed specification. Therefore, Applicants respectfully request that this objection be withdrawn.

III. Rejection of claims 70 and 72 under 35 U.S.C. § 101

The Examiner has rejected claims 70 and 72 under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter. The Examiner asserts that these claims read on products of nature. Applicants have amended claims 70 and 72 to recite a "recombinantly produced" glycopolypeptide. Accordingly, Applicants respectfully request that this rejection be withdrawn.

IV. Rejection of claims 69-72 under 35 U.S.C. § 103(a)

The Examiner has rejected claims 69-72 under 35 U.S.C. § 103(a) as being unpatentable over Chamberlin & Dean, 87 Proc. Natl. Acad. Sci. 6014 (1990) in view of Kinloch et al., 92 Proc. Natl. Acad. Sci. USA 263 (1995). Chamberlin & Dean is relied on in this action for describing a human ZP3 protein comprising the amino acid sequence of the claimed SEQ ID NO: 2. The Examiner admits that Chamberlin & Dean do not describe a recombinantly produced polypeptide and do not describe a glycopolypeptide. Kinloch et al. is relied on in this action for describing a recombinantly produced ZP3 polypeptide and glycoprotein in order to create and test mutant ZP3 proteins for sperm-binding activity. The Examiner asserts that it would have been obvious for a person of ordinary skill in the art to combine the ZP3 amino acid sequence of Chamberlin & Dean with the method of making recombinant ZP3 protein of Kinloch et al. in order to produce a recombinant ZP3 polypeptide or glycopolypeptide. The Examiner further asserts that Kinloch et al. provide motivation by teaching the importance of a specific portion of ZP3 glycopolypeptide located in the carboxy-terminal end of both mouse and human ZP3 protein and that Kinloch et al. sets forth a method of producing mouse and chimeric human ZP3 protein. This rejection is respectfully traversed for the reasons described below.

To properly make a rejection under 35 U.S.C. § 103, the Examiner has the initial burden of establishing a *prima facie* case of obviousness. Meeting this burden requires the Examiner to show first, that the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process. Second, the Examiner must establish that the prior art would have revealed that in so making or carrying out

the claimed process, those of ordinary skill in the art would have had a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be found in the prior art, not in Applicants' disclosure. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). Furthermore, it is well settled that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination. *In re Geiger*, 2 U.S.P.Q.2d 1276 (Fed. Cir. 1987).

The Chamberlin and Dean and Kinloch et al. references do not describe or suggest a recombinantly produced polypeptide or glycopolypeptide expressed by a human ovarian cell comprising SEQ ID NO: 2 or a conservatively substituted amino acid sequence thereof, wherein such polypeptide binds human spermatozoa, as recited in amended claims 69-72. It is alleged that Kinloch describes the concept of creating mutant ZP3 protein and subsequently testing for sperm-binding activity as a well-known and routine practice. (Office Action at 8.) However, Kinloch et al. discloses the production of a recombinant hZP3 protein in embryonal carcinoma ("EC") cells, resulting in *inactive* hZP3. (See p. 263, col. 1, lines 35-40). Therefore, the inactive hZP3 produced in Kinloch does not bind human spermatozoa.

Unlike the Chamberlin & Dean and Kinloch references, as discussed in the specification at page 7, lines 26-28, the inventors of the present invention have surprisingly discovered that "human rZP3 made by non-human ovarian cell lines such as a CHO cell line, while having the same amino acid sequence as human ZP3, are not active with human eggs because of their carbohydrate component." There is no description or suggestion in Kinloch et al. of using human ovarian cells to express a *biologically active* human ZP3. Moreover, the Examiner asserts that

the "recitation of the intended use of the claimed invention must result in a structural different between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." As clearly addressed in the specification, the structural differences between the human ZP3 polypeptide expressed by a human ovarian cell than the human ZP3 polypeptide expressed in Kinloch are clear – those according to the present invention are biologically active and bind to human spermatozoa; those according to Kinloch are biologically inactive. These activities make clear that there are structural differences between the two.

It seems that what the Examiner is attempting to do is to assert that the characteristics of the claimed product and the Kinloch product are inherent. However, the rejection is not based on anticipation, which would allow one to argue inherency. Rather, the rejection is based on obviousness for which an inherency argument is inappropriate.

Finally, Applicants respectfully dispute that Kinloch provides the motivation to combine the peptide of Chamberlin & Dean to be recombinantly produced in the cells disclosed in Kinloch. To the contrary, Kinloch shows that recombinant production of hZP3 is neither a simple matter nor routine. Indeed, the researcher's own unsuccessful attempt to produce recombinant hZP3 is telling. The extrapolation of Kinloch's failure to produce active recombinant hZP3 to remotely suggest success in human ovarian cells is based upon improper hindsight reasoning. At best, Kinloch provides only the motivation to try to see whether or not hZP3 can be recombinantly produced in human ovarian cells. However, as consistently held at the Federal Circuit, the motivation to try does not provide the requisite reasonable expectation of success to uphold an obviousness rejection. Instead, nothing in Chamberlin & Dean and Kinloch leads one to reasonably expect success in producing a recombinantly produced polypeptide or

glycopolypeptide expressed by a human ovarian cell that binds human spermatozoa according to amended claims 69-72. Withdrawal of this rejection is respectfully requested.

V. Rejection of claims 71 and 72 under 35 U.S.C. § 103(a)

The Examiner has rejected claims 71 and 72 under 35 U.S.C. § 103(a) as being unpatentable over Chamberlin & Dean, 87 Proc. Natl. Acad. Sci. 6014 (1990) in view of Kinloch et al., 92 Proc. Natl. Acad. Sci. USA 263 (1995) and Rosiere & Wasserman. The Examiner admits that Chamberlin & Dean do not describe a conservatively substituted amino acid sequence of SEQ ID NO: 2. However, Rosiere & Wasserman are relied on in this action for describing the general location in mouse ZP3 protein sequence responsible for sperm-binding activity in that they identify a particular peptide fragment derived from the carboxyl-terminal end of the mouse ZP3 protein. The Examiner also relies upon Kinloch et al. for allegedly extending the knowledge of the art by pointing to the exact amino acid residues of human ZP3 likely responsible for sperm binding and describing site-directed ZP3 mutant proteins in order to map the mouse ZP3 sperm binding site. Therefore, the Examiner asserts that it would have been obvious for a person of ordinary skill in the art to combine the peptide of Chamberlin & Dean to the ZP3 mutants of Kinloch et al. to provide a peptide of SEQ ID NO: 2 with conservative amino acid substitutions.

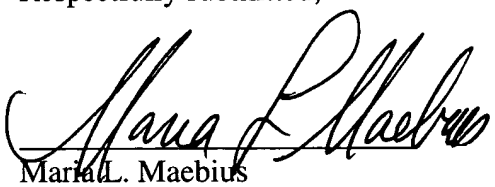
The deficiencies of Chamberlin & Dean and Kinloch et al. were addressed above. Rosiere & Wasserman do not remedy the deficiencies as they do not describe or suggest a recombinantly produced polypeptide or glycopolypeptide expressed by a human ovarian cell consisting of SEQ ID NO: 2 or a conservatively substituted amino acid sequence thereof, as

recited in amended claims 71 and 72. Rosiere & Wasserman merely purified and isolated mZP3 using either papain or V8 protease. Accordingly, Applicants assert that none of the references, whether alone or in combination, teach or suggest the presently claimed invention of amended claims 71 and 72. Applicants respectfully request that this rejection be withdrawn.

VI. CONCLUSION

In view of the foregoing remarks, Applicants believe that the application is in condition for allowance. However, if the Examiner disagrees, he is encouraged to call the undersigned at the number listed below in order to expedite the prosecution of this application.

Respectfully submitted,



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